

5 CLAIMS

WHAT IS CLAIMED IS:

1. An isolated nucleic acid molecule comprising a polynucleotide having a nucleotide sequence selected from the group consisting of:
 - (a) a polynucleotide fragment of SEQ ID NO:1 or a polynucleotide fragment of the cDNA sequence included in ATCC Deposit No: PTA-2966, which is hybridizable to SEQ ID NO:41;
 - (b) a polynucleotide encoding a polypeptide fragment of SEQ ID NO:42 or a polypeptide fragment encoded by the cDNA sequence included in ATCC Deposit No: PTA-2966, which is hybridizable to SEQ ID NO:41;
 - (c) a polynucleotide encoding a polypeptide domain of SEQ ID NO:42 or a polypeptide domain encoded by the cDNA sequence included in ATCC Deposit No: PTA-2966, which is hybridizable to SEQ ID NO:41;
 - (d) a polynucleotide encoding a polypeptide epitope of SEQ ID NO:42 or a polypeptide epitope encoded by the cDNA sequence included in ATCC Deposit No: PTA-2966, which is hybridizable to SEQ ID NO:41;
 - (e) a polynucleotide encoding a polypeptide of SEQ ID NO:42 or the cDNA sequence included in ATCC Deposit No: PTA-2966, which is hybridizable to SEQ ID NO:41, having biological activity;
 - (f) a polynucleotide which is a variant of SEQ ID NO:41;
 - (g) a polynucleotide which is an allelic variant of SEQ ID NO:41;
 - (h) an isolated polynucleotide comprising nucleotides 473 to 2464 of SEQ ID NO:41, wherein said nucleotides encode a polypeptide corresponding to amino acids 2 to 665 of SEQ ID NO:42 minus the start codon;
 - (i) an isolated polynucleotide comprising nucleotides 470 to 2464 of SEQ ID NO:41, wherein said nucleotides encode a polypeptide corresponding to amino acids 1 to 665 of SEQ ID NO:109 including the start codon;
 - (j) a polynucleotide which represents the complimentary sequence (antisense) of SEQ ID NO:41;
 - (k) a polynucleotide fragment of SEQ ID NO:108 or a polynucleotide fragment of the cDNA sequence included in ATCC Deposit No: PTA-3434, which is hybridizable to SEQ ID NO:108;

- 5 (l) (b) a polynucleotide encoding a polypeptide fragment of SEQ ID NO:109 or a polypeptide fragment encoded by the cDNA sequence included in ATCC Deposit No: PTA-3434, which is hybridizable to SEQ ID NO:108;
- (m) a polynucleotide encoding a polypeptide domain of SEQ ID NO:109 or a polypeptide domain encoded by the cDNA sequence included in ATCC Deposit No: 10 PTA-3434, which is hybridizable to SEQ ID NO:108;
- (n) a polynucleotide encoding a polypeptide epitope of SEQ ID NO:109 or a polypeptide epitope encoded by the cDNA sequence included in ATCC Deposit No: PTA-3434, which is hybridizable to SEQ ID NO:108;
- (o) a polynucleotide encoding a polypeptide of SEQ ID NO:109 or the cDNA 15 sequence included in ATCC Deposit No: PTA-3434, which is hybridizable to SEQ ID NO:108, having biological activity;
- (p) a polynucleotide which is a variant of SEQ ID NO:108;
- (q) a polynucleotide which is an allelic variant of SEQ ID NO:108;
- (r) an isolated polynucleotide comprising nucleotides 541 to 2532 of SEQ ID 20 NO:108, wherein said nucleotides encode a polypeptide corresponding to amino acids 2 to 665 of SEQ ID NO:109 minus the start codon;
- (s) an isolated polynucleotide comprising nucleotides 538 to 2532 of SEQ ID NO:108, wherein said nucleotides encode a polypeptide corresponding to amino acids 1 to 665 of SEQ ID NO:109 including the start codon;
- 25 (t) a polynucleotide which represents the complimentary sequence (antisense) of SEQ ID NO:108;
- (u) an isolated polynucleotide comprising nucleotides 541 to 1443 of SEQ ID NO:108, wherein said nucleotides encode a polypeptide corresponding to amino acids 2 to 302 of SEQ ID NO:109 minus the start codon;
- 30 (v) an isolated polynucleotide comprising nucleotides 538 to 1443 of SEQ ID NO:108, wherein said nucleotides encode a polypeptide corresponding to amino acids 1 to 302 of SEQ ID NO:109 including the start codon;
- (w) a polynucleotide fragment of SEQ ID NO:149 or a polynucleotide fragment of the cDNA sequence included in ATCC Deposit No: XXXXX, which is 35 hybridizable to SEQ ID NO:149;

- 5 (x) a polynucleotide encoding a polypeptide fragment of SEQ ID NO:150 or a polypeptide fragment encoded by the cDNA sequence included in ATCC Deposit No: PTA-XXXXXX, which is hybridizable to SEQ ID NO:149;
- (y) a polynucleotide encoding a polypeptide domain of SEQ ID NO:150 or a polypeptide domain encoded by the cDNA sequence included in ATCC Deposit No:
- 10 PTA-XXXXXX, which is hybridizable to SEQ ID NO:149;
- (z) a polynucleotide encoding a polypeptide epitope of SEQ ID NO:150 or a polypeptide epitope encoded by the cDNA sequence included in ATCC Deposit No: PTA-XXXXXX, which is hybridizable to SEQ ID NO:149;
- (aa) a polynucleotide encoding a polypeptide of SEQ ID NO:150 or the
- 15 cDNA sequence included in ATCC Deposit No: XXXXXX, which is hybridizable to SEQ ID NO:149, having biological activity;
- (bb) a polynucleotide which is a variant of SEQ ID NO:149;
- (cc) a polynucleotide which is an allelic variant of SEQ ID NO:149;
- (dd) an isolated polynucleotide comprising nucleotides 631 to 2448 of SEQ
- 20 ID NO:149, wherein said nucleotides encode a polypeptide corresponding to amino acids 2 to 607 of SEQ ID NO:150 minus the start codon;
- (ee) an isolated polynucleotide comprising nucleotides 628 to 2448 of SEQ ID NO:149, wherein said nucleotides encode a polypeptide corresponding to amino acids 1 to 607 of SEQ ID NO:150 including the start codon;
- 25 (ff) a polynucleotide which represents the complimentary sequence (antisense) of SEQ ID NO:149;
- (gg) a polynucleotide fragment of SEQ ID NO:151 or a polynucleotide fragment of the cDNA sequence included in ATCC Deposit No: XXXXXX, which is hybridizable to SEQ ID NO:151;
- 30 (hh) a polynucleotide encoding a polypeptide fragment of SEQ ID NO:152 or a polypeptide fragment encoded by the cDNA sequence included in ATCC Deposit No: XXXXXX, which is hybridizable to SEQ ID NO:151;
- (ii) a polynucleotide encoding a polypeptide domain of SEQ ID NO:152 or a polypeptide domain encoded by the cDNA sequence included in ATCC Deposit No:
- 35 XXXXXX, which is hybridizable to SEQ ID NO:151;

- 5 (jj) a polynucleotide encoding a polypeptide epitope of SEQ ID NO:152 or a polypeptide epitope encoded by the cDNA sequence included in ATCC Deposit No: XXXXX, which is hybridizable to SEQ ID NO:151;
- (kk) a polynucleotide encoding a polypeptide of SEQ ID NO:152 or the cDNA sequence included in ATCC Deposit No: XXXXX, which is hybridizable to
- 10 SEQ ID NO:151, having biological activity;
- (ll) a polynucleotide which is a variant of SEQ ID NO:151;
- (mm) a polynucleotide which is an allelic variant of SEQ ID NO:151;
- (nn) an isolated polynucleotide comprising nucleotides 92 to 538 of SEQ ID NO:151, wherein said nucleotides encode a polypeptide corresponding to amino acids
- 15 2 to 150 of SEQ ID NO:152 minus the start codon;
- (oo) an isolated polynucleotide comprising nucleotides 89 to 538 of SEQ ID NO:151, wherein said nucleotides encode a polypeptide corresponding to amino acids 1 to 150 of SEQ ID NO:152 including the start codon;
- (pp) a polynucleotide which represents the complimentary sequence
- 20 (antisense) of SEQ ID NO:151; and
- (qq) a polynucleotide capable of hybridizing under stringent conditions to any one of the polynucleotides specified in (a)-(pp), wherein said polynucleotide does not hybridize under stringent conditions to a nucleic acid molecule having a nucleotide sequence of only A residues or of only T residues.
- 25 2. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises a nucleotide sequence encoding a human phosphatase protein.
3. A recombinant vector comprising the isolated nucleic acid molecule of claim 1.
- 30 4. The recombinant host cell of claim 3 comprising vector sequences.
5. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of:
- (a) a polypeptide fragment of SEQ ID NO:42 or the encoded sequence included in ATCC Deposit No: PTA-2966;
- 35 (b) a polypeptide fragment of SEQ ID NO:42 or the encoded sequence included in ATCC Deposit No: PTA-2966, having biological activity;

- 5 (c) a polypeptide domain of SEQ ID NO:42 or the encoded sequence included in ATCC Deposit No: PTA-2966;
- (d) a polypeptide epitope of SEQ ID NO:42 or the encoded sequence included in ATCC Deposit No: PTA-2966;
- (e) a full length protein of SEQ ID NO:42 or the encoded sequence included in
10 ATCC Deposit No: PTA-2966;
- (f) a variant of SEQ ID NO:42;
- (g) an allelic variant of SEQ ID NO:42;
- (h) a species homologue of SEQ ID NO:42;
- (i) a polypeptide comprising amino acids 2 to 665 of SEQ ID NO:42, wherein
15 said amino acids 2 to 665 comprise a polypeptide of SEQ ID NO:42 minus the start methionine;
- (j) a polypeptide comprising amino acids 1 to 665 of SEQ ID NO:42; and
- (k) a polypeptide encoded by the cDNA contained in ATCC Deposit No. PTA-2966;
- 20 (l) a polypeptide fragment of SEQ ID NO:109 or the encoded sequence included in ATCC Deposit No: PTA-3434;
- (m) a polypeptide fragment of SEQ ID NO:109 or the encoded sequence included in ATCC Deposit No: PTA-3434, having biological activity;
- (n) a polypeptide domain of SEQ ID NO:109 or the encoded sequence
25 included in ATCC Deposit No: PTA-3434;
- (o) a polypeptide epitope of SEQ ID NO:109 or the encoded sequence included in ATCC Deposit No: PTA-3434;
- (p) a full length protein of SEQ ID NO:109 or the encoded sequence included in ATCC Deposit No: PTA-3434;
- 30 (q) a variant of SEQ ID NO:109;
- (r) an allelic variant of SEQ ID NO:109;
- (s) a species homologue of SEQ ID NO:109;
- (t) a polypeptide comprising amino acids 2 to 665 of SEQ ID NO:109, wherein said amino acids 2 to 665 comprise a polypeptide of SEQ ID NO:109 minus
35 the start methionine;
- (u) a polypeptide comprising amino acids 1 to 665 of SEQ ID NO:109;

- 5 (v) a polypeptide encoded by the cDNA contained in ATCC Deposit No. PTA-3434;
- (w) a polypeptide fragment of SEQ ID NO:150 or the encoded sequence included in ATCC Deposit No: XXXXX;
- (x) a polypeptide fragment of SEQ ID NO:150 or the encoded sequence
10 included in ATCC Deposit No: XXXXX, having biological activity;
- (y) a polypeptide domain of SEQ ID NO:150 or the encoded sequence included in ATCC Deposit No: XXXXX;
- (z) a polypeptide epitope of SEQ ID NO:150 or the encoded sequence included in ATCC Deposit No: XXXXX;
- 15 (aa) a full length protein of SEQ ID NO:150 or the encoded sequence included in ATCC Deposit No: XXXXX;
- (bb) a variant of SEQ ID NO:150;
- (cc) an allelic variant of SEQ ID NO:150;
- (dd) a species homologue of SEQ ID NO:150;
- 20 (ee) a polypeptide comprising amino acids 2 to 607 of SEQ ID NO:150, wherein said amino acids 2 to 607 comprise a polypeptide of SEQ ID NO:150 minus the start methionine;
- (ff) a polypeptide comprising amino acids 1 to 607 of SEQ ID NO:150;
- (gg) a polypeptide encoded by the cDNA contained in ATCC Deposit No.
25 XXXX;
- (hh) a polypeptide fragment of SEQ ID NO:152 or the encoded sequence included in ATCC Deposit No: XXXXX;
- (ii) a polypeptide fragment of SEQ ID NO:152 or the encoded sequence included in ATCC Deposit No: XXXXX, having biological activity;
- 30 (jj) a polypeptide domain of SEQ ID NO:152 or the encoded sequence included in ATCC Deposit No: XXXXX;
- (kk) a polypeptide epitope of SEQ ID NO:152 or the encoded sequence included in ATCC Deposit No: XXXXX;
- (ll) a full length protein of SEQ ID NO:152 or the encoded sequence included
35 in ATCC Deposit No: XXXXX;
- (mm) a variant of SEQ ID NO:152;

- 5 (nn) an allelic variant of SEQ ID NO:152;
 (oo) a species homologue of SEQ ID NO:152;
 (pp) a polypeptide comprising amino acids 2 to 150 of SEQ ID NO:152,
 wherein said amino acids 2 to 150 comprise a polypeptide of SEQ ID NO:152 minus
 the start methionine;
 10 (qq) a polypeptide comprising amino acids 1 to 150 of SEQ ID NO:152;
 and
 (rr) a polypeptide encoded by the cDNA contained in ATCC Deposit No.
 XXXX.

- 15 6. The isolated polypeptide of claim 5, wherein the full length protein
 comprises sequential amino acid deletions from either the C-terminus or the N-
 terminus.
 7. An isolated antibody that binds specifically to the isolated polypeptide
 of claim 5.
 8. A recombinant host cell that expresses the isolated polypeptide of
 20 claim 15
 9. A method of making an isolated polypeptide comprising:
 (a) culturing the recombinant host cell of claim 8 under conditions such that
 said polypeptide is expressed; and
 (b) recovering said polypeptide.
 25 10. The polypeptide produced by claim 9.
 11. A method for preventing, treating, or ameliorating a medical condition,
 comprising administering to a mammalian subject a therapeutically effective amount
 of the polypeptide of claim 5 or the polynucleotide of claim 1.
 12. A method of diagnosing a pathological condition or a susceptibility to
 30 a pathological condition in a subject comprising:
 (a) determining the presence or absence of a mutation in the polynucleotide of
 claim 1; and
 (b) diagnosing a pathological condition or a susceptibility to a pathological
 condition based on the presence or absence of said mutation.
 35 13. A method of diagnosing a pathological condition or a susceptibility to
 a pathological condition in a subject comprising:

5 (a) determining the presence or amount of expression of the polypeptide of claim 5 in a biological sample; and

(b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or amount of expression of the polypeptide.

14. A process for making polynucleotide sequences encoding a gene product having altered phosphatase activity comprising,
 10 a) shuffling a nucleotide sequence of claim 1,
 b) expressing the resulting shuffled nucleotide sequences and,
 c) selecting for altered phosphatase activity as compared to the phosphatase activity of the gene product of said unmodified nucleotide sequence.

15 15. A shuffled polynucleotide sequence produced from the process of claim 14.

16. An isolated nucleic acid molecule consisting of a polynucleotide having a nucleotide sequence selected from the group consisting of:

- (a) a polynucleotide encoding a polypeptide of SEQ ID NO:42;
- 20 (b) an isolated polynucleotide comprising nucleotides 473 to 2464 of SEQ ID NO:41, wherein said nucleotides encode a polypeptide corresponding to amino acids 2 to 665 of SEQ ID NO:42 minus the start codon;
- (c) an isolated polynucleotide comprising nucleotides 473 to 2464 of SEQ ID NO:41, wherein said nucleotides encode a polypeptide corresponding to
 25 amino acids 2 to 665 of SEQ ID NO:42 including the start codon;
- (d) a polynucleotide encoding the BMY_HPP5 polypeptide encoded by the cDNA clone contained in ATCC Deposit No. PTA-2966;
- (e) a polynucleotide which represents the complimentary sequence (antisense) of SEQ ID NO:41;
- 30 (f) a polynucleotide encoding a polypeptide of SEQ ID NO:109;
- (g) an isolated polynucleotide comprising nucleotides 473 to 2464 of SEQ ID NO:41, wherein said nucleotides encode a polypeptide corresponding to amino acids 2 to 665 of SEQ ID NO:42 minus the start codon;
- (h) an isolated polynucleotide comprising nucleotides 473 to 2464 of
 35 SEQ ID NO:41, wherein said nucleotides encode a polypeptide corresponding to amino acids 2 to 665 of SEQ ID NO:42 including the start codon;

- 5 (i) a polynucleotide encoding the RET31 polypeptide encoded by the cDNA clone contained in ATCC Deposit No. PTA-3434;
- (j) a polynucleotide which represents the complimentary sequence (antisense) of SEQ ID NO:109;
- (k) an isolated polynucleotide comprising nucleotides 541 to 1443 of
10 SEQ ID NO:108, wherein said nucleotides encode a polypeptide corresponding to amino acids 2 to 302 of SEQ ID NO:109 minus the start codon;
- (l) an isolated polynucleotide comprising nucleotides 538 to 1443 of SEQ ID NO:108, wherein said nucleotides encode a polypeptide corresponding to amino acids 1 to 302 of SEQ ID NO:109 including the start codon;
- 15 (m) a polynucleotide encoding a polypeptide of SEQ ID NO:150;
- (n) an isolated polynucleotide comprising nucleotides 631 to 2448 of SEQ ID NO:149, wherein said nucleotides encode a polypeptide corresponding to amino acids 2 to 607 of SEQ ID NO:150 minus the start codon;
- (o) an isolated polynucleotide comprising nucleotides 628 to 2448 of
20 SEQ ID NO:149, wherein said nucleotides encode a polypeptide corresponding to amino acids 2 to 607 of SEQ ID NO:150 including the start codon;
- (p) a polynucleotide encoding the BMY_HPP5 polypeptide encoded by the cDNA clone contained in ATCC Deposit No. XXXXX;
- (q) a polynucleotide which represents the complimentary sequence
25 (antisense) of SEQ ID NO:149;
- (r) a polynucleotide encoding a polypeptide of SEQ ID NO:152;
- (s) an isolated polynucleotide comprising nucleotides 92 to 538 of SEQ ID NO:151, wherein said nucleotides encode a polypeptide corresponding to amino acids 2 to 150 of SEQ ID NO:152 minus the start codon;
- 30 (t) an isolated polynucleotide comprising nucleotides 89 to 538 of SEQ ID NO:151, wherein said nucleotides encode a polypeptide corresponding to amino acids 2 to 150 of SEQ ID NO:152 including the start codon;
- (u) a polynucleotide encoding the BMY_HPP5 polypeptide encoded by the cDNA clone contained in ATCC Deposit No. XXXXX; and
- 35 (v) a polynucleotide which represents the complimentary sequence (antisense) of SEQ ID NO:151.

- 5 17. The isolated nucleic acid molecule of claim 16, wherein the polynucleotide comprises a nucleotide sequence encoding a human phosphatase protein.
18. A recombinant vector comprising the isolated nucleic acid molecule of claim 16.
- 10 19. A recombinant host cell comprising the recombinant vector of claim 18.
20. An isolated polypeptide consisting of an amino acid sequence selected from the group consisting of:
- 15 (a) a polypeptide fragment of SEQ ID NO:42 having phosphatase activity;
- (b) a polypeptide domain of SEQ ID NO:42 having phosphatase activity;
- (c) a full length protein of SEQ ID NO:42;
- (d) a polypeptide corresponding to amino acids 2 to 665 of SEQ ID NO:42, wherein said amino acids 2 to 665 comprise a polypeptide of SEQ ID NO:42 minus the start methionine;
- 20 (e) a polypeptide corresponding to amino acids 1 to 665 of SEQ ID NO:42;
- (f) a polypeptide encoded by the cDNA contained in ATCC Deposit No. PTA-2966;
- (g) a polypeptide fragment of SEQ ID NO:109 having phosphatase
- 25 activity;
- (h) a polypeptide domain of SEQ ID NO:109 having phosphatase activity;
- (i) a full length protein of SEQ ID NO:109;
- (j) a polypeptide corresponding to amino acids 2 to 665 of SEQ ID NO:109, wherein said amino acids 2 to 665 comprise a polypeptide of SEQ ID
- 30 NO:109 minus the start methionine;
- (k) a polypeptide corresponding to amino acids 1 to 665 of SEQ ID NO:109;
- (l) a polypeptide encoded by the cDNA contained in ATCC Deposit No. PTA-3434;

- 5 (m) a polypeptide corresponding to amino acids 2 to 302 of SEQ ID NO:109, wherein said amino acids 2 to 302 comprise a polypeptide of SEQ ID NO:109 minus the start methionine;
- (n) a polypeptide corresponding to amino acids 1 to 302 of SEQ ID NO:109;
- (o) a polypeptide fragment of SEQ ID NO:150 having phosphatase activity;
- 10 (p) a polypeptide domain of SEQ ID NO:150 having phosphatase activity;
- (q) a full length protein of SEQ ID NO:150;
- (r) a polypeptide corresponding to amino acids 2 to 607 of SEQ ID NO:150, wherein said amino acids 2 to 607 comprise a polypeptide of SEQ ID NO:150 minus the start methionine;
- 15 (s) a polypeptide corresponding to amino acids 1 to 607 of SEQ ID NO:150;
- (t) a polypeptide encoded by the cDNA contained in ATCC Deposit No. XXXXX;
- (u) a polypeptide fragment of SEQ ID NO:152 having phosphatase activity;
- (v) a polypeptide domain of SEQ ID NO:152 having phosphatase activity;
- 20 (w) a full length protein of SEQ ID NO:152;
- (x) a polypeptide corresponding to amino acids 2 to 150 of SEQ ID NO:152, wherein said amino acids 2 to 150 comprise a polypeptide of SEQ ID NO:152 minus the start methionine;
- (y) a polypeptide corresponding to amino acids 1 to 150 of SEQ ID NO:152;
- 25 and
- (z) a polypeptide encoded by the cDNA contained in ATCC Deposit No. XXXX.

21. A method of phosphorylating a protein comprising the step of
30 incubating said protein with the isolated polypeptide of claim 5.

22. The method for preventing, treating, or ameliorating a medical condition of claim 21, wherein the medical condition is a proliferative disorder.

23. A computer for producing a three-dimensional representation of a molecule or molecular complex, wherein said molecule or molecular complex
35 comprises the structural coordinates of a member of the group consisting of

- (a) BMY_HPP1 model provided in Figure 28 in accordance with Table VIII

- 5 (b) BMY_HPP2 model provided in Figure 32 in accordance with Table IX;
and
(c) BMY_HPP5 model provided in Figure 38 in accordance with Table X,
wherein said computer comprises:
- 10 (a) A machine-readable data storage medium, comprising a data storage
material encoded with machine readable data, wherein the data is defined by the set of
structure coordinates of the model;
(b) a working memory for storing instructions for processing said machine-
readable data;
- 15 (c) a central-processing unit coupled to said working memory and to said
machine-readable data storage medium for processing said machine readable data into
said three-dimensional representation; and
(d) a display coupled to said central-processing unit for displaying said three-
dimensional representation.

20 24. A method for identifying a mutant with altered biological properties,
function, or activity of a member of the group consisting of:

- (a) BMY_HPP1;
(b) BMY_HPP2; and
25 (c) BMY_HPP5,
Wherein said method comprises the steps of:
(a) using a model of said polypeptide according to the structural coordinates
of said model to identify amino acids to mutate; and
(b) mutating said amino acids to create a mutant protein with altered
30 biological function or properties.

25. A method for designing or selecting compounds as potential
modulators of a member of the group consisting of:

- (a) BMY_HPP1;
35 (b) BMY_HPP2; and
(c) BMY_HPP5,

Wherein said method comprises the steps of:

- (a) identifying a structural or chemical feature of said member using the structural coordinates of said member; and
- (b) rationally designing compounds that bind to said feature.

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